April 1985:891–7

REVIEWS

Asynchronous (Segmental Early) Relaxation of the Left Ventricle

WILLIAM H. GAASCH, MD, FACC, ALVIN S. BLAUSTEIN, MD, OSCAR H. L. BING, MD

Boston, Massachusetts

Segmental early relaxation, a form of left ventricular asynchrony, refers to lengthening of a myocardial segment before mitral valve opening. This phenomenon may occur in normal and diseased hearts; when it is seen in a diseased ventricle it may occur in either the abnormally contracting segment or the normal segment. Experimental data indicate that altered loading conditions, especially nonuniform distribution of load or functional inhomogeneities (as may occur with regional ischemia), or both, may result in asynchronous relaxation of the left ventricle.

(J Am Coll Cardiol 1985;5:891–7)

Myocardial relaxation can be considered as the process by which myofibrils return to their initial resting tension and length. In the intact heart a decrease in pressure normally precedes chamber filling; however, segmental lengthening during the period of decreasing isovolumic pressure occasionally results in what has been called "segmental early relaxation" (1). The purpose of this report is to summarize the published data on early relaxation, review some of the factors known to influence left ventricular relaxation and suggest how these factors might cause this interesting phenomenon.

Segmental Early Relaxation Phenomenon

The segmental early relaxation phenomenon has been defined as localized early outward motion of the left ventricular wall, usually occurring in a normally contracting segment and accompanied by simultaneous inward motion in another segment (1). This asynchronous motion occurs after the ventricle has achieved its smallest systolic volume; the term "early" refers to the observation that a segment of the left ventricular wall appears to lengthen and move outward before the mitral valve opens. Although others (2) had previously described similar patterns of unusual wall motion, it was Altieri et al. (1) who first defined and used the term "segmental early relaxation phenomenon." Later, Hamby et al. (3) refined the description by correlating individual cineangiographic frames with the electrocardiogram and central aortic pressure recordings. They noted that the outward motion sometimes began before aortic valve closure and confirmed that the phenomenon was established well before the onset of ventricular filling (before mitral valve opening).

Relation to coronary artery disease. The early relaxation phenomenon is seen most frequently in the anterior wall of the ventricle. Perhaps because of this, attempts have been made to establish a relation between segmental early relaxation and the presence of left anterior descending coronary artery disease. However, the phenomenon has been seen in patients with and without coronary disease, and when coronary artery narrowings were present, there was usually a poor correlation between the distribution of the stenosed vessel and the segment exhibiting early relaxation (3,4). Gibson and coworkers (5–7) examined late systolic wall movements during the interval between minimal cavity size and mitral valve opening (utilizing cineangiograms and echocardiograms) and constructed detailed three-dimensional maps of endocardial motion that allowed localized abnormalities to be identified. These studies, which provide the most quantitative available data regarding regional wall motion during the so-called isovolumic relaxation period, clearly document early outward wall motion in areas supplied by normal coronary arteries; this outward motion was accompanied by inward motion in regions supplied by diseased vessels. In contrast, Wilson et al. (8) observed a close correlation between anterior wall segmental early relaxation and disease of the left anterior descending coronary artery.

From the Department of Medicine, Division of Cardiology, Tufts University School of Medicine and the Veterans Administration Medical Center, Boston, Massachusetts. This study was supported in part by Grants HL28377 and HL20552 from the National Heart, Lung, and Blood Institute, Bethesda, Maryland; Grant 81-850 from the American Heart Association, Dallas, Texas and funds from the Medical Research Service of the Veterans Administration, Washington, D.C. Dr. Bing was the recipient of Career Development Award 00072 from the National Institutes of Health, Bethesda, Maryland. Manuscript received July 10, 1984; revised manuscript received October 30, 1984, accepted November 6, 1984.

Address for reprints: William H. Gaasch, MD, Cardiology Section, Veterans Administration Medical Center, 150 South Huntington Avenue, Boston, Massachusetts 02130.

0735-1097/85/$3.30

JACC Vol. 5, No. 4
April 1985:891–7

These discordant clinical observations on the relation of segmental early relaxation to the presence or absence of coronary disease have not yet been resolved.

Relation to rate of left ventricular pressure decrease and loading conditions. Although early relaxation is generally regarded as a regional or localized phenomenon, variables based on the rate of left ventricular pressure decrease may also be affected. In this regard, Ludbrook et al. (9) compared data from patients with synchronous wall motion with data from a group exhibiting segmental early relaxation. Although the distribution of normal and diseased ventricles was similar in both groups, several measures of isovolumic relaxation rate indicated prolonged pressure decrease in ventricles exhibiting asynchronous "protodiastolic segmental wall motion." These observations are consonant with those of Alam et al. (10), who found an increased isovolumic relaxation time in patients with this phenomenon. Ludbrook et al. also made the important observation that isometric exercise exaggerates the phenomenon, whereas nitroglycerin attenuates it. The segmental early relaxation phenomenon, therefore, appears to be a dynamic phenomenon that is influenced by acute alterations in left ventricular loading conditions.

Quantitative data on regional wall motion. In studies designed to quantitate regional wall motion in human subjects, Klausner et al. (11) performed frame by frame analysis of left ventricular cineangiograms and found a systematic inhomogeneity in normal ventricles. Their data indicate that anterior wall lengthening occurs earlier and more rapidly than that seen in inferior wall segments. Thus, it seems possible that the early relaxation phenomenon could, in some patients, be an exaggeration of normal inhomogeneity. With the exception of the detailed studies by Gibson and coworkers (5–7) of left ventricular wall motion, it should be recognized that the published reports on early relaxation consist almost entirely of qualitative angiographic observations and that quantitative measurements of regional wall motion will be necessary if we are to understand the entire spectrum of asynchronous contraction-relaxation of the left ventricle.

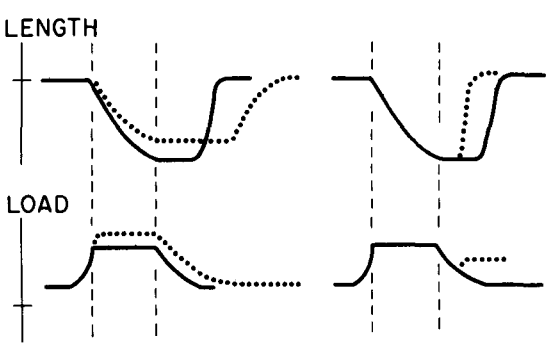
Mechanisms. Any hypothesis regarding the mechanism or mechanisms responsible for the segmental early relaxation phenomenon must account for its occurrence in normal and diseased ventricles, its dynamic behavior and its segmental nature. The explanation of Hamby et al. (3) implicating unrecognized localized conduction disturbances remains unsupported, but it is possible that local electrical delays can exist despite a normal electrocardiographic QRS complex. The suggestion that a small increment in ventricular volume occurs during aortic valve closure does not account for the segmental nature of the phenomenon (4). Thus, the descriptive nature of the existing studies provides little insight into the mechanisms responsible for the early relaxation. In the next section of this report, we will review some of the factors that influence myocardial relaxation and discuss the manner in which these factors might contribute to asynchronous (segmental early) relaxation of the left ventricle. As will be seen, there appears to be no single explanation for the phenomenon; in fact, it is likely that several factors, alone or in combination, may under different circumstances produce segmental early relaxation.

Myocardial Relaxation

Myocardial relaxation, the process by which myofibrils return to their initial tension and length, is influenced by an interplay of multiple factors. These include the process of deactivation (the reversal of biochemical events that lead to activation-contraction) and the prevailing loads on the myocardium. The loading conditions *early* in the contraction (12), the history or time course of load *during* contraction (13) as well as loads applied *late* in contraction (14) all may influence the time course of relaxation; the effects of early and late loads are shown in Figure 1. The process of myocardial relaxation, which is initiated and proceeds according to interactions between load and deactivation, is modulated by neurohumeral and metabolic influences (that is, ischemia or hypoxia) as well as by pharmacologic interventions and changes in the synchrony of contraction-relaxation (14–16).

Prolonged isovolumic relaxation, ventricular pressure and afterload. We and others (17–19) previously demonstrated a direct relation between left ventricular systolic pressure and the isovolumic relaxation time constant during a variety of experimental hemodynamic interventions that impose afterload changes early in the cardiac cycle. In these studies, the systemic administration of vasopressors, which

Figure 1. Diagrammatic representation of the effect of early and late increments in myocardial load. The control records are shown as **solid lines** and the effects of an increment in load are shown as **dashed lines**. In the **left panels**, load is increased early in contraction; less shortening occurs, the onset of lengthening is delayed and lengthening rate is reduced. In contrast, when the load is applied late, during force decline, the muscle lengthens prematurely and the rate of lengthening is increased (**right panels**). This response to a late increment in load is an example of "load-dependent relaxation."



increase afterload early and throughout systole, causes a slower time course of isovolumic pressure decrease; vasodilators result in a more rapid isovolumic pressure decrease. The finding of prolonged isovolumic relaxation at higher left ventricular afterload (increased systolic pressure and length) is analogous to the observation of Parmley and Sonnenblick (20) in isolated muscle, but should be distinguished from the concept of Brutsaert et al. (14) of "load-dependent relaxation." Essentially, this distinction depends on the difference between the effects of load alterations imposed early in the contraction cycle (which can still reset the force potential to a new level) and of alterations in the prevailing load late in contraction and throughout relaxation (when readjustment of force potential is unlikely). Late in contraction, the number of crossbridges cannot be increased to support an additional load; as a result, relaxation is induced prematurely and its time course is more rapid. These speculations are supported by the observation that left ventricular isovolumic pressure decrease occurs earlier and is more rapid when an increment in pressure (21) or length (22) is applied late in systole. The example shown in Figure 2 illustrates the effect of a load (volume) increment on pressure decrease in the intact dog heart.

The phenomenon of load-dependent relaxation as defined by Brutsaert et al. (14) is based on a substantial body of experimental data which indicate that myocardial lengthening occurs early when an increment in load is applied near the end of contraction. Thus, the application of a load during the late phases of contraction can not only affect isovolumic pressure decline (see foregoing), but it may also influence lengthening. Recognizing that the segmental early relaxation phenomenon (early lengthening) occurs well before mitral valve opening, how can our current understanding of myocardial relaxation contribute to a better understanding of the mechanisms responsible for the phenomenon? First, consider the factors that might promote early rapid relaxation of myofibrils: what might cause a late load increment and thereby promote early rapid relaxation? Second, recall the localized nature of the phenomenon: if load-dependent relaxation is to be implicated in the genesis of segmental early relaxation, inhomogeneity must exist within the wall of the ventricle. In the next section, we will discuss hemodynamic factors which may be at least partially responsible for segmental early relaxation; this will be followed by a discussion of left ventricular inhomogeneity.

Hemodynamic Factors

Reflected pressure waves. Reflected waves, which depend in part on the properties of the arterial system, may influence instantaneous ventricular load during ejection by changing the aortic pressure waveform. The shape of the ascending aorta pressure wave and its relation to aortic input impedance has been studied in patients without heart disease by Murgo et al. (23). In their studies, a late systolic ("secondary") increase in pressure was associated with a more oscillatory impedance spectrum than was observed in patients whose early systolic pressure exceeded late systolic pressure. These observations appeared to be due to differences in reflections within the arterial tree, and not to differences in cardiac function.

The amplitude of a late systolic (reflected) increase in pressure can be modified by external compression of the femoral arteries as well as pharmacologic or other short-term interventions; minute to minute, or even beat to beat, changes in the ascending aorta pressure waveform can create

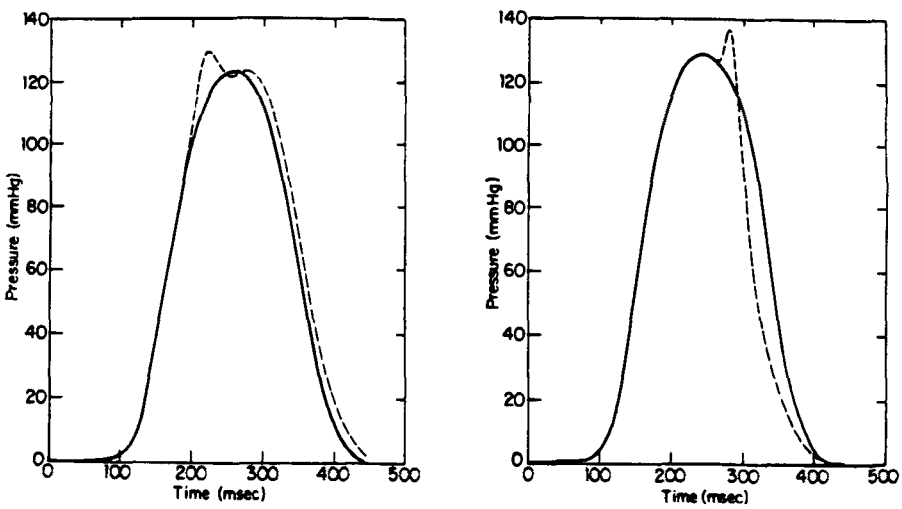


Figure 2. Effect of an abrupt volume increment on the time course of left ventricular pressure. These data were obtained using a computer-controlled servo pump connected to the apex of an intact dog left ventricle. The **solid lines** are control isovolumic beats and the **dashed lines** are intervention (quick stretch) beats. In the **left panel**, the volume increment (6 ml of blood) is given early in contraction. In the **right panel**, the volume increment is given late in contraction. The early volume infusion caused a slight delay in the onset of pressure decrease. By comparison, the volume increment given in late systole produces a quite different result. Here the pressure decrease is earlier and much more rapid; peak negative dP/dt increased from 1,742 mm Hg/s in the control beat to 3,005 mm Hg/s in the intervention beat. This response to a late systolic stretch is a manifestation of "load-dependent relaxation" in the intact heart.

alterations in the time course of left ventricular systolic pressure. Such an abrupt increase in late systolic pressure is analogous to the application of a load increment late in the contraction of an isolated muscle preparation. In this manner a late systolic reflected wave could produce early or premature relaxation of the ventricle (load-dependent relaxation). This speculation is consistent with the observation that isometric exercise and vasopressors tend to exaggerate segmental early relaxation, whereas nitroglycerin tends to reduce it (9). However, regional inhomogeneities in left ventricular stiffness or other factors must also be present if one is to explain the segmental nature of the early relaxation phenomenon.

Aortic valve closure. During aortic valve closure a small portion of the left ventricular stroke volume returns to the ventricle. Apparently, this increment in left ventricular volume at the very end of systole can amount to as much as 10% of the total stroke volume. Thus, if the stroke volume is calculated (that is, angiographically) from the end diastolic and the smallest late systolic cine frames, stroke volume will be overestimated (4). The factors that influence the magnitude of this volume increment are not defined, but it is possible that relative pressure transients in the aorta and left ventricle as well as the pliability of the valve leaflets are important in this regard. If this is true, long-term changes in aortic valve structure and short-term changes in central hemodynamics can influence the magnitude of this physiologic aortic regurgitation.

This small increase in left ventricular volume at the end of systole is analogous to a load or length increment late in the contraction sequence of isolated cardiac muscle; the concept of load-dependent relaxation then explains how the process of left ventricular relaxation (lengthening) is initiated early, that is, near the time of aortic valve closure. Similar to the effect of reflected pressure waves, this increment in left ventricular volume shold have a global effect on relaxation and, thus, it alone would not be expected to produce segmental or asynchronous changes.

Coronary perfusion. Pure alterations in coronary blood flow may be responsible for changes in left ventricular systolic function and diastolic compliance. These alterations, which are said to be due to an erectile or hydraulic effect, may occur in the absence of metabolic changes (24–26). Presumably, increased coronary perfusion pressure and coronary blood flow result in coronary vascular engorgement (erectile effect), which in turn causes an increase in perivascular fiber stretch and an increase in fiber tension; conversely, a short-term decrease in coronary blood volume may reduce fiber stretch. Immediately after aortic valve closure, while left ventricular pressure is decreasing, an abrupt increase in coronary blood flow occurs (27). Owing in part to the rapid decrease in chamber pressure (and intramyocardial pressure), coronary blood volume rapidly increases and measured left ventricular wall volume (wall thickness) increases. Thus, after aortic valve closure, abrupt coronary engorgement may result in a lengthening force which is applied to the myocardial fibers that surround engorged vessels; in this manner the erectile effect might contribute to early relaxation.

This mechanism is especially appealing because it might explain the observation that the segmental early relaxation phenomenon is more common in the distribution of the left than of the right coronary artery (4). In the normal heart, left coronary flow reaches a peak immediately after aortic valve closure, whereas right coronary flow shows less variation throughout the cardiac cycle. Importantly, in coronary artery disease, vascular obstruction might well limit the degree of vascular engorgement and fiber stretch distal to the stenosis, thus allowing for inhomogeneous distribution of the late systolic load (stretch). This hypothesis is consonant with the observation that the early relaxation phenomenon is generally seen in segments supplied by a patent vessel.

Inhomogeneity

Acute myocardial ischemia. It is generally accepted that myocardial ischemia impairs or slows the relaxation process (11). Ischemia also influences the load dependency of relaxation and, if it is localized to a segment of the left ventricle, a complex situation of functional, temporal and spacial inhomogeneity develops. Thus, the notion that segmental early relaxation is due to ischemia itself is a difficult hypothesis to test. There is, however, indirect evidence that mild ischemia (or hypoxia), or ischemia of very brief duration, is associated with the early relaxation phenomenon if the ischemic (weak) segment is placed in series with a normal (strong) segment.

Wiegner et al. (28) studied the interaction of myocardial segments of different strengths by modeling the contraction of strong (normal) and weak (hypoxic) muscle in series. They studied this interaction by using a computer that stored the force record of a normal contraction. The hypoxic muscle then was subjected to the normal force pattern and in effect was contracting in series with normal myocardium. Data from a typical experiment are shown in Figure 3. The first change in the length record of the hypoxic muscle (5 minutes) is an early onset of lengthening that increases progressively during the hypoxic period. The important observation relative to the present discussion is the premature onset of lengthening in the hypoxic segment that occurs as a result of greater force in the normal segment at that time.

Brief ischemia. Early segmental ischemia in the intact dog heart is also associated with the early onset of segment lengthening (Fig. 4) (29). Within 30 seconds of coronary occlusion, the segment shows an early lengthening pattern that is remarkably similar to the isolated muscle record shown in Figure 3. Early lengthening is also seen in the

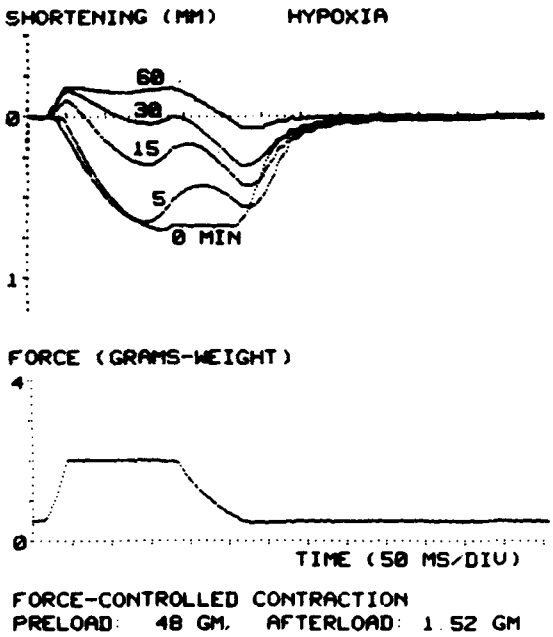


Figure 3. Interaction between a muscle subjected to hypoxia for 60 minutes (length record in **upper panel**) and a "normal" muscle (force record in **lower panel**). The earliest change is a premature onset of lengthening (5 minutes), and as hypoxia progresses, there is less total shortening; by 60 minutes the hypoxia muscle demonstrates "systolic" lengthening which coincides with the period of force development in the normal muscle. During the period of force decline (normal muscle, below), the hypoxic muscle manifests late systolic shortening. See text for details.

marginal segment at 50 seconds. It appears, therefore, that the early onset of lengthening may occur in hypoxic or ischemic muscle when the weak muscle interacts with strong or normal muscle. Similar patterns of early segmental lengthening have been observed clinically during percutaneous transluminal balloon coronary angioplasty (30). When left ventricular cineangiograms are obtained during very brief periods of balloon inflation, an early outward endocardial motion can be seen in the segment supplied by the coronary vessel undergoing angioplasty. The acute development of segmental early relaxation during transluminal angioplasty (brief period of ischemia) is analogous to the experimental data presented in Figures 3 and 4.

Severe or prolonged ischemia. When the ischemia is more severe or prolonged, the ischemic segment develops pansystolic lengthening (paradoxical bulge) with late systolic or protodiastolic shortening; the normal segment commonly shows a prominent early onset of lengthening which is temporally related to protodiastolic shortening in the ischemic segment. Analysis of multiple segment length recordings from animals subjected to regional ischemia reflects a broad spectrum of changes, but several familiar patterns are commonly observed (31); the pansystolic lengthening and protodiastolic shortening in the ischemic segment are associated with early lengthening in the control segment (Fig. 5). These experimental findings are consonant with the clinical observations that, in patients with coronary heart disease, segmental early relaxation is usually present in the segment with normal motion and is rare in the abnormally contracting segment.

Late shortening of ischemic or hypoxic myocardium is probably due to a combination of persistent contractile activity and recoil of passive elastic elements within the muscle. Length of the normal segment during this period is determined by the difference in relative rates of force decline in the two segments. If contractile force declines more rapidly in the normal segment than in the ischemic segment, the normal segment will show early lengthening. This tug of war between functionally disparate segments will complicate any analysis of left ventricular wall motion.

Long-term segmental disorders. Many patients with coronary heart disease exhibit segmental hypokinesia or other localized contraction abnormalities on a long-term basis. Much of the left ventricular myocardium remains normal in these patients and, thus, global function of the left ventricle is influenced by interactions among segments (28). The normal or strong segment influences the shortening pattern of the weak segment, and vice versa. These interactions are probably responsible, at least in part, for the multiple patterns of abnormal length transients seen in clinical and experimental studies of left ventricular wall motion (31,32). In addition to the effects of functional inhomogeneity, spatial nonuniformity (regional variations in end-diastolic fiber length or sarcomere length) could mimic the effects of weak and strong myocardium in series. Likewise, temporal dispersion of excitation-contraction (as may occur in conduction disturbances) may also cause changes in the rate of isovolumic pressure decline or lengthening, or both (15,33). It appears, therefore, that nonhomogeneous contraction of the left ventricle results in asynchronous relaxation; such inhomogeneity can result in the combination of early lengthening in a normal segment and late shortening in a weak segment.

Conclusions

Within the context of this review, early relaxation refers to myocardial lengthening before the mitral valve opens. However, this terminology is imprecise. First, the term "relaxation" (which refers to the process by which myofibrils return to their initial tension and length) should not be used interchangeably with fiber lengthening alone. Second, the onset of relaxation is difficult to define and, partly for this reason, the term "early" may be questioned. Muscle lengthening before mitral valve opening can be considered early, but isometric relaxation before mitral valve opening is certainly not early. Thus, the more general term "asyn-

JACC Vol. 5, No. 4
April 1985:891–7

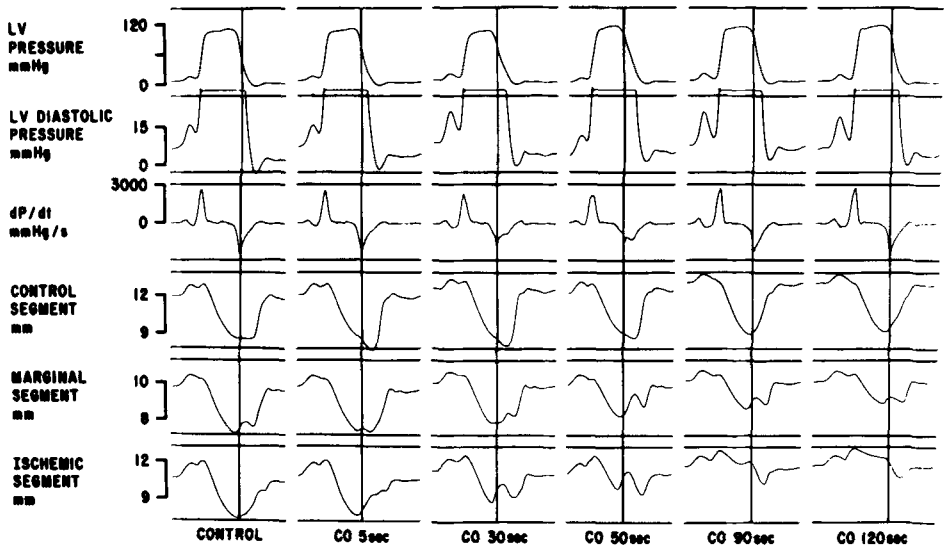


Figure 4. Effects of coronary occlusion (CO) on contraction-relaxation of myocardial segments in the zone of ischemia, in a segment on the border of the ischemic zone ("marginal") and a remote segment ("control"). For reference, a **vertical line** has been drawn at the instant of peak negative dP/dt, which occurs near the time of aortic valve closure. Before coronary occlusion, lengthening in both control and ischemic zones begins after the **vertical reference line**. Within 5 seconds of coronary occlusion, the ischemic segment shows early lengthening. As ischemia progresses, late systolic shortening develops similar to the pattern seen in Figure 3. In the control segment, the onset of lengthening precedes the reference line at 90 seconds of ischemia; the premature onset of lengthening in the normal segment is temporally related to late systolic shortening in the ischemic segment. This early and rapid lengthening in the normal segment is similar to that seen in patients with the segmental early relaxation phenomenon. (Reproduced from Theroux et al. [29] by permission of the American Heart Association, Inc.)

chronous relaxation" might be preferable to "segmental early relaxation."

Despite these problems, our current understanding of the process of myocardial relaxation provides some insight into several mechanisms that might be responsible for asynchronous relaxation. For example, in the normal heart, the hydraulic (erectile) effect of coronary perfusion could contribute to segmental early relaxation in the distribution of the left anterior descending coronary artery. However, in the presence of an obstructing left anterior descending coronary artery lesion, mild ischemia could be responsible for early relaxation of the anterior wall, whereas more severe ischemia could result in early relaxation of the opposing wall. Segmental interactions resulting from uncoordinated contraction-relaxation (due to scar or local conduction delay) could also be responsible for the early relaxation phe-

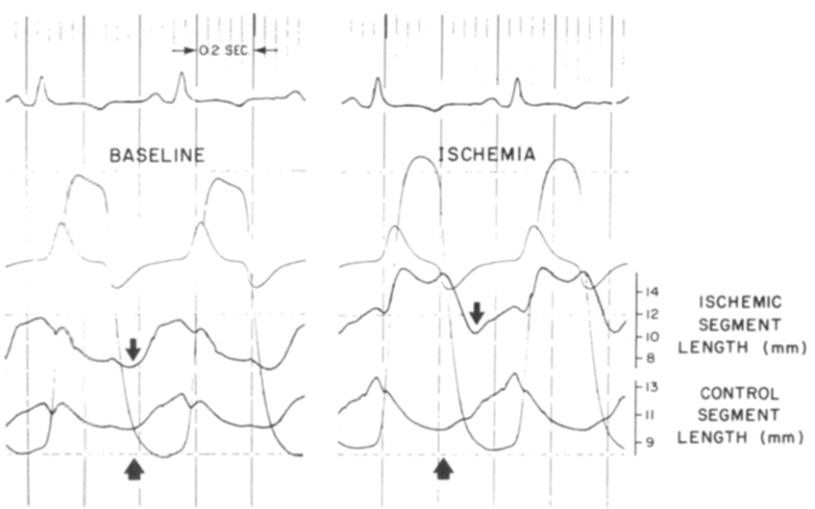


Figure 5. Interaction between control and ischemic segments before (baseline) and after (ischemia) 5 minutes of coronary occlusion. The **arrows** denote the onset of lengthening. In the baseline state, the onset of lengthening is synchronous in the two segments; it occurs well after peak negative dP/dt at a time when left ventricular pressure is approaching its minimum. With ischemia, there is early systolic lengthening followed by late shortening as the ischemic segment is first loaded during early contraction, and then unloaded during the period of pressure decline (Fig. 3). The onset of lengthening in the two segments (which was nearly simultaneous in the baseline state) is substantially different during ischemia. The ischemic segment lengthens 30 ms later, whereas the onset of lengthening in the control segments is 80 ms earlier (both relative to baseline). These dynamic changes in the onset of lengthening are analogous to those seen in the segmental early relaxation phenomenon.

nomenon. It appears, therefore, that segmental early relaxation may be caused by a variety of factors, some of which may be fixed and long-term while others may be dynamic and vary from minute to minute or even beat to beat. Under some circumstances, a single mechanism may be responsible, but sometimes an interplay of several hemodynamic or other factors may be necessary to produce the segmental early relaxation phenomenon.

References

1. Altieri PI, Wilt SM, Leighton RF. Left ventricular wall motion during the isovolumic relaxation period. Circulation 1973;48:499–505.
2. Gooch AS, Vicencio F, Maranhaov V, Goldberg H. Arrhythmias and left ventricular asynergy in the prolapsing mitral leaflet syndrome. Am J Cardiol 1972;29:611–5.
3. Hamby RI, Aintablian A, Tabrah F, Reddy K, Wisoff G. Late systolic bulging of left ventricle in patients with angina pectoris: a form of asynchronous contraction. Chest 1974;65:169–75.
4. Ruttley MS, Admas DF, Cohn PF, Abrams HL. Shape and volume changes during "isovolumetric relaxation" in normal and asynergic ventricles. Circulation 1974;50:306–16.
5. Gibson DG, Prewitt TA, Brown DJ. Analysis of left ventricular wall movement during isovolumic relaxation and its relation to coronary artery disease. Br Heart J 1976;38:1010–9.
6. Upton MT, Gibson DG, Brown DJ. Echocardiographic assessment of abnormal left ventricular relaxation in man. Br Heart J 1976;38:1001–9.
7. Chen W, Gibson DG. Relation of isovolumic relaxation to left ventricular wall movement in man. Br Heart J 1979;42:51–6.
8. Wilson CS, Krueger S, Forker AD, Weaver WF. Correlation between segmental early relaxation of the left ventricular wall and coronary occlusive disease. Am Heart J 1975;89:474–9.
9. Ludbrook PA, Byrne JD, Tiefenbrunn AJ. Association of asynchronous protodiastolic segmental wall motion with impaired left ventricular relaxation. Circulation 1980;64:1201–11.
10. Alam SE, Tansey WA, Cameron A, Kemp HG. Asynchronous ventricular relaxation: an angiographic temporal analysis of asynchronous left ventricular relaxation in man. Am J Cardiol 1979;43:41–6.
11. Klausner S, Blair TJ, Bulawa WF, Jeppson GM, Jensen RL, Clayton PD. Quantitative analysis of segmental wall motion throughout systole and diastole in the normal human left ventricle. Circulation 1982;65:580–90.
12. Gaasch WH, Blaustein AS, Andrias CW, Donahue RP, Avitall B. Myocardial relaxation. II. Hemodynamic determinants of rate of left ventricular isovolumic pressure decline. Am J Physiol 1980;239:H1-6.
13. Hori M, Inoue M, Fukunami M, et al. Influence of ejection timing on left ventricular relaxation in isolated canine heart (abstr). Circulation 1982;66(suppl II):II-304.
14. Brutsaert DL, Housemans PR, Goethals MA. Dual control of relaxation: its role in the ventricular function in the mammalian heart. Circ Res 1980;47:637–52.
15. Blaustein AS, Gaasch WH. Myocardial relaxation. VI. Effects of beta adrenergic tone and asynchrony on LVP and relaxation rate. Am J Physiol 1983;244:H417–22.
16. Brutsaert DL, Rademakers FE, Sys SU. Triple control of relaxation: implications in cardiac disease. Circulation 1984;69:190–6.
17. Gaasch WH, Blaustein AS, Adam D. Myocardial relaxation. IV. Mechanical determinants of the time course of left ventricular pressure decline during isovolumic relaxation. Eur Heart J 1980;1(suppl A):111–7.
18. Karliner JS, LeWinter M, Mahler F, Engler R, O'Rourke RA. Pharmacologic and hemodynamic influences on the rate of isovolumic left ventricular relaxation in the normal conscious dog. J Clin Invest 1977;60:511–2.
19. Raff GL, Glantz SA. Volume loading slows left ventricular isovolumic relaxation rate: evidence of load-dependent relaxation in the intact dog heart. Circ Res 1981;48:813–24.
20. Parmley WW, Sonnenblick EH. Relation between mechanism of contraction and relaxation in mammalian cardiac muscle. Am J Physiol 1969;216:1084–91.
21. Goethals MA, Kersschot IE, Claes VA, Hermans CF, Jageneau AH, Brutsaert DL. Influence of abrupt pressure increments on left ventricular relaxation (abstr). Am J Cardiol 1980;45:392.
22. Ariel Y. Studies in Cardiac Mechanics Using a Servo Pump. PhD Thesis. Harvard University, Cambridge, Massachusetts, 1982.
23. Murgo JP, Westerhof N, Giolma JP, Altobelli SA. Aortic input impedance in normal man: relationship to pressure wave forms. Circulation 1980;62:105–16.
24. Salisbury PF, Cross CE, Rieben PA. Influence of coronary artery pressure upon myocardial elasticity. Circ Res 1960;8:794–800.
25. Gaasch WH, Bing OHL, Franklin A, Rhodes D, Bernard SA, Weintraub RN. The influence of acute alterations in coronary blood flow on left ventricular diastolic compliance and wall thickness. Eur J Cardiol 1978;7:147–61.
26. Vogel WM, Apstein CS, Briggs LL, Gaasch WH, Ahn J. Acute alterations in left ventricular diastolic chamber stiffness. Role of the erectile effect of coronary artery pressure and flow in normal and damaged hearts. Circ Res 1982;51:465–78.
27. Rubio R, Berne RM. Regulation of coronary blood flow. Prog Cardiovasc Dis 1975;18:105–22.
28. Wiegner AW, Allen GJ, Bing OHL. Weak and strong myocardium in series: implications for segmental dysfunction. Am J Physiol 1978;235:H776–83.
29. Theroux P, Ross J Jr, Franklin D, Kemper WS, Sasayama S. Regional myocardial function in the conscious dog during acute coronary occlusion and responses to morphine, propranolol, nitroglycerine and lidocaine. Circulation 1976;53:302–14.
30. Sigwart U, Grbic M, Essinger A, Fischer A, Morin D, Sadeghi H. Myocardial function in man during acute coronary balloon occlusion (abstr). Circulation 1982;66(suppl II):II-86.
31. Nakamura Y, Takahashi M, Hayashi J, et al. Protection of ischemic myocardium with coenzyme Q10. Cardiovasc Res 1982;16:127–32.
32. Herman MV, Heinle RA, Klein MD, Gorlin R. Localized disorders in myocardial contraction: asynergy and its role in congestive heart failure. N Engl J Med 1967;277:222–32.
33. Zile MR, Blaustein AS, Thomas MJ, Gaasch WH. Left ventricular relaxation and filling: effect of systolic load on peak segment lengthening rate (abstr). Clin Res 1984;32:219A.